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Effect of exogenous ketones as an adjunct to low-calorie diet on metabolic markers

Submission date
13/10/2025

Recruitment status
No longer recruiting

Registration date
23/10/2025

Overall study status
Completed

Last Edited
23/10/2025

Condition category
Nutritional, Metabolic, Endocrine

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
Many adults carry extra body fat, which can harm their health. Losing weight by eating fewer calories often reduces both fat and muscle. Losing muscle can slow metabolism and make it harder to keep weight off. This study looks at whether taking a ketone supplement called beta-hydroxybutyrate, or BHB, can help people lose more fat while keeping more muscle during a modest calorie-reduced diet. The main aim is to learn whether adding BHB to a reduced-calorie diet improves body composition by lowering fat mass and protecting lean mass, without lowering resting metabolic rate. A second aim is to see how the supplement affects common health markers in blood, such as LDL cholesterol and liver enzymes, and whether there are any safety concerns. Earlier research suggests BHB may help the body use fat for fuel and may protect muscle during calorie restriction. This trial is designed to test these ideas in a careful, blinded way.

Who can participate?
Healthy adult volunteers aged between 18 and 45 years

What does the study involve?
The study lasts 8 weeks. Adults with overweight or obesity follow a simple meal plan that reduces daily calories by about 500. The plan is roughly 40 percent carbohydrate, 30 percent protein, and 30 percent fat. People are randomly assigned to one of two groups. One group takes BHB mineral salts. The other group takes a placebo that looks and tastes the same. Neither the participants nor the study team doing the measurements know who is in which group until after the study ends.

Participants attend a screening visit to make sure it is safe to join. At the start and end of the 8 weeks, they come to the lab for measurements. These include body weight, body fat and muscle using a DEXA scan, resting metabolic rate using a breathing test, blood pressure, and standard blood tests. They also record what they eat on several days and have brief weekly check-ins to support the meal plan.

What are the possible benefits and risks of participating?
Possible benefits

Participants may lose body weight and body fat during the 8-week program.
Participants may keep more muscle while losing fat, which can help maintain their resting metabolism.
Your LDL cholesterol and some liver enzyme levels may improve.
Participants will receive health measurements, including DEXA body composition, resting metabolic rate, blood pressure, and blood tests, which some people find informative and motivating.
Participants will get basic nutrition guidance and regular check-ins that can support healthy habits.
Please note that benefits cannot be guaranteed. Some people may not see changes.

Possible risks and burdens
Supplement side effects. BHB mineral salts can sometimes cause stomach upset, nausea, diarrhea, or a bad taste. Because they contain minerals like sodium and potassium, there is a small chance of fluid shifts or changes in electrolytes, especially if taken in excess.
Diet discomfort. Eating fewer calories may lead to hunger, tiredness, irritability, headache, or temporary difficulty concentrating, especially in the first weeks.
Blood draws. Risks include brief pain, bruising, lightheadedness, or rarely infection at the needle site.
DEXA scan. This test uses a very low dose of X-ray. The radiation exposure is minimal and considered safe for adults, but it is avoided in pregnancy.
Time and travel. You will spend time on two clinic visits, keep food records, take the study product twice a day, and respond to weekly check-ins.
Allergies or intolerance. Very rarely, people may be sensitive to ingredients in the supplement or placebo.
No guaranteed improvement. You may not lose weight or may lose some muscle despite efforts.
Confidentiality. Your personal data will be protected to the extent allowed by law and ethics rules. There is a very small risk of loss of confidentiality, which the team works to prevent.

Where is the study run from?
Brigham Young University, USA

When is the study starting and how long is it expected to run for?
January 2019 to October 2025

Who is funding the study?
Ketone Labs, USA

Who is the main contact?
Benjamin Bikman, bikman@byu.edu.

Contact information

Type(s)
Public, Scientific, Principal investigator

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Additional identifiers

Study information

Scientific Title
Effect of exogenous ketones as an adjunct to low-calorie diet on metabolic markers

Acronym
EXKET

Study objectives
To test the effects of a ketone supplement on weight loss in a low-calorie diet.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 05/01/2019, Advarra Institutional Review Board (IRB) (3815 S. Capital of Texas Hwy, Suite 320, Austin, TX 78704, United States of America; +1 512 326 3001 ; cirbi@advarra.com), ref: KETAD-001-2018

Study design
Randomized placebo-controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Influencing weight loss with a low-calorie diet.

Interventions
Study Procedures:

Visit 1 (screening):

• The experimental procedures used in the study will be communicated to subjects verbally and in writing. Subjects will have an opportunity to ask questions about the study. Written informed

consent will be obtained.
• Medical history, physical, routine safety blood work (uric acid, metabolic panel, CBC & lipid panel), and baseline diet. Female participants will take a urinary pregnancy test. If subjects are unable to get pregnant (have had tubes tied, etc.), they must bring documentation that they cannot get pregnant. Subjects who are enrolled on the study will be reminded not to exercise for 48 hours and abstain from caffeine and alcohol 24 hours before reporting to the laboratory.

Visit 2 (week 0):

• Body weight and vital signs.
• Anchored VAS subscales for evaluating appetite, cravings for sweet foods, mental clarity, mood, and fatigue (Baseline, 60 min, 120 mins, and post).
• RMR (resting metabolic rate) via indirect calorimetry.
• DEXA scan for body composition measurements of fat mass, fat-free mass, and visceral adipose tissue.
• Blood draw: insulin level

Visit 3 (week 8):

• Body weight and vital signs.
• Anchored VAS subscales for appetite, cravings for sweet foods, mental clarity, mood, and fatigue. (Baseline, 60 min, 120 mins, and post).
• RMR (resting metabolic rate) via indirect calorimetry.
• DEXA for body composition measurements of fat mass, fat-free mass, and visceral adipose tissue.
• Blood draw: safety (uric acid, metabolic panel, CBC, lipid panel) and insulin.

DIET:

• All subjects will be placed on a “Zone” type diet that provides approximately 500 kcals per day less than their estimated energy requirements (via the Mifflin St. Jeor equation). The research dietitian will meet with each subject to explain the proper procedures for recording dietary intake and provide examples of the types of foods they can consume.
• Each subject’s baseline diet (3 days: two weekdays & one weekend day) will be analyzed via NutriBase IX (Clinical Edition) to determine its energy and macronutrient content.
• Additional 3-day diet records will be analyzed before the last day of testing (i.e. during week 8) to verify that eating habits remained consistent throughout the study.

EXERCISE TRAINING AND PHYSICAL ACTIVITY:

• Subjects will be asked to increase their habitual physical activity to 30 minutes of walking exercise at least 3 days per week.
• To monitor compliance with the exercise regimen, each subject will document their walking exercise in a training log that will be brought with them at each visit.
• Each subject’s physical activity will be assessed via a standardized questionnaire at baseline and again on the last day of testing (during the week 8 visit).

SUPPLEMENTATION:

• After qualifying for the study, subjects will be matched according to gender (sex) and BMI before being randomly assigned to receive, in a double-blinded manner, either Kegenix-Prime, goBHB, and Prime D Plus or the placebo.

• Randomization was through a randomly generated computer code, assigning each participant to a group.
• Subjects randomized to the active product (i.e. exogenous ketones) groups will consume the manufacturer's recommended dose (i.e. 1 scoop in the morning, 1 scoop in the evening) every day for eight weeks. Subjects randomized into the placebo group will consume an isoenergetic /isocaloric amount of carbohydrate (~ 80 calories).
• Supplements will be prepared in powdered form, matched for flavor and consistency, and packaged in coded generic containers for double-blind administration.
• Compliance with the supplementation regimen will be monitored by daily logs.

BLOOD SAMPLES:

There will be 3 blood draws. The blood draws will be performed by trained study staff using a needle stick in your arm. The total amount of blood drawn at each visit will be about 32 mL (4 tablespoons). For comparison, the standard blood donation is about 480 mL (two cups).

Intervention Type
Supplement

Primary outcome(s)
Body mass changes were measured using a dual-energy X-ray absorptiometry (DXA) scanner at the beginning and end of the study

Key secondary outcome(s))
Blood markers were measured using ELISA and dot blot at the beginning and end of the study

Completion date
31/10/2025

Eligibility

Key inclusion criteria
1. BMI between 27 and 35 kg/m²
2. Stable weight (±2.3 kg in the previous 30 days)
3. Classified as normotensive (systolic <140 mmHg, diastolic <90 mmHg, resting heart rate <90 beats/min)

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit

46 years

Sex
All

Total final enrolment
51

Key exclusion criteria
1. Pregnancy, nursing
2. Any history of metabolic disease (e.g., diabetes, thyroid disorders), cardiovascular disease, hepatic or renal dysfunction, autoimmune or neurological conditions
3. Individuals taking dietary supplements or medications known to alter body weight, metabolism, or hormone levels within four weeks of study initiation

Date of first enrolment
01/03/2019

Date of final enrolment
31/12/2021

Locations

Countries of recruitment
United States of America

Study participating centre
The Center for Applied Health Sciences
6570 Seville Dr.
Canfield
United States of America
44406

Sponsor information

Organisation
Brigham Young University

ROR
https://ror.org/047rhhm47

Funder(s)

Funder type
Industry

Funder Name
Ketone Labs

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analyzed during the current study will be available upon request from Benjamin Bikman, bikman@byu.edu.
- Type of data: Clinical outcomes
- Timing: After publication and upon request
- Consent: Consent was obtained from each participant
- Data: All participants were assigned a study subject number upon enrollment
- Restrictions: None.

IPD sharing plan summary
Available on request